

Inventor's statement

I refer to the USPTO's Office Action dated April 28, 2008, in which the examiner mentions that according to his opinion, Groups I and II of the invention, as defined by the examiner, do not share a common inventive technical feature over the prior art in the view of Young et al. (Aus. J. Zool. 45(4):423-433; 1997).

The examiner noted that the abstract and page 425 seem the most relevant passages to him.

As the inventor of the present invention and a person skilled in the art, I would like to submit the following:

The publication by Young et al. discloses cellular components identified in the milk of the tammar wallaby. Said components include macrophages, neutrophils, lymphocytes and other vacuolated mononuclear cells (see abstract).

According to page 425 in combination with figure 5, eosinophilic cells were also found in the milk samples. Eosinophilic cells, as all other cells mentioned in the abstract and concerned in this paper, are immune cells, which are terminally differentiated cells. Stem cells, however, are pluri- or multipotent cells in the body, which have the ability to differentiate into various different cell types.

The following sentence of lines 4-5 of page 425 makes absolutely no sense in the eyes of a person skilled in the art: *"These cells closely resembled blast cells and may be primitive stem cells or epithelial in origin."*

This sentence is full of severe contradictions, which is why a person skilled in the art would ignore it completely, especially in view of figure 5.

1. Eosinophilic cells cannot closely resemble blast cells.

Their size and morphology are fundamentally different.

A blast cell is an immature, undifferentiated cell of a proliferative compartment in a cell lineage that normally represents up to 5% of the cells in the bone marrow, i.e. a usually large immature precursor of a blood cell in the earliest stage of development. Blast cells are

characterized by a relatively large nucleus with a spongy, loose network of chromatin and several nucleoli; mitochondria are extremely fine and delicate.

In contrast, eosinophilic cells are fully differentiated immune cells (leukocytes). Their cell size and shape mimic that of neutrophils. There is no way a person skilled in the art would believe that eosinophilic cells resemble blast cells. Eosinophilic cells generally have a bi-lobed nucleus which may appear like multiple nuclei. The cytoplasm may look transparent because of fine granules.

In addition, blast cells are much smaller ($< 8\ \mu\text{m}$) than fully differentiated eosinophilic cells as shown in figure 5 to be about $15\ \mu\text{m}$.

2. Eosinophilic cells cannot be primitive stem cells.

Eosinophilic cells are terminally differentiated immune cells (leukocytes) in contrast to stem cells, which are undifferentiated, totipotent or at least multipotent cells. Furthermore, stem cells are tiny, i.e. $5\text{--}6\ \mu\text{m}$, while eosinophilic cells are shown in figure 5 to have a size of about $15\ \mu\text{m}$.

Even if one read the sentence as meaning “primitive stem cells in origin”, which would give the sentence a different meaning, this part of the sentence wouldn’t provide any knowledge either to a person skilled in the art, since every cell in a human body originates from a primitive stem cell. Leukocytes are all produced and derived from a multipotent cell in the bone marrow known as a hematopoietic stem cell.

3. Eosinophilic cells cannot be epithelial in origin.

They have completely different functions, locations and sizes from each other.

Eosinophilic cells, as mentioned above, are immune cells flowing and circulating in the blood. Eosinophils have a role in the protective immunity against certain parasites but also contribute to the inflammation that occurs in allergic disorders.

In comparison, epithelial cells are cells originating from a basal layer of the epithelium. They do not circulate in the blood, but are closely packed cells forming the epithelium. The epithelium is a tissue composed of layers of cells that line the cavities and surfaces of structures throughout the body. It is also the type of tissue of which many glands are formed. Epithelium lines both the outside (skin) and the inside cavities and lumen of bodies. The cells

originate in the basal layer of the epithelium and then migrate across the upper layers to the surface of the tissue, where they are shed. Functions of epithelial cells include secretion, absorption, protection, transcellular transport, sensation detection, and selective permeability. Furthermore, epithelial cells are very large in size, i.e. 30-50 μm , while eosinophilic cells are shown in figure 5 to have a diameter size of about 15 μm . This is another sign pointing to the incorrectness of the statement on page 425 of Young et al..

Based on the information on how the cells were prepared for mounting them on slides for photography (as mentioned on page 424), the person skilled in the art can tell that the cells in the figures should be exhibiting their natural size and shape in figure 5, as they have not been manipulated. The possibility that the cells are larger or smaller than normal can therefore be ruled out here.

In summary, besides being a speculative hypothetical statement as to where the cells found in the milk of the tammar wallaby might originate from, the statement in paragraph 2 of page 425 is simply incorrect and misleading and this is immediately recognized by the person skilled in the art.

The statement as to how which other cell-types the cells resembled or where they might originate from is not based on any evidence. The evidence given in figure 5 of the publication speaks *against* the statement and confirms the critical reader's doubts concerning its truth. A person skilled in the art with general knowledge background would never mistake a cell of about 15 μm , as shown in figure 5, for a stem cell, which normally has a size of about 5-6 μm .

By saying that the cells found were eosinophils, besides the macrophages, neutrophils and lymphocytes found, the reader skilled in the art derives from the publication only the information that various different immune cells were found in the milk of the researched species.

4. No stem-cell-specific isolation techniques were used in the isolation method

The findings of the Young et al. publication did not include any novel methodology for isolation of stem cells, and as such differs markedly from the claims in the submitted patent.

I therefore hereby submit that I respectfully disagree with the examiner's statement that the publication by Young et al. discloses or suggests the finding of stem cells in mammary secretion. Based on this finding, the two groups I and II are based on a common general inventive concept and should not be separated from each other in the application.

Sincerely,

A handwritten signature in black ink, appearing to read 'M Cregan', with a horizontal line extending from the end of the signature.

Mark D. Cregan, PhD.

Crawley, Australia, August 20, 2008